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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,380	08/02/2001	Charles Mark Ensor	PHOE-0061	7237

7590 10/29/2003

Gwilym John Owen Attwell
WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103

EXAMINER

PATTERSON, CHARLES L. JR.

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/921,380	Applicant(s) ENSOR ET AL.	
	Examiner Charles L. Patterson, Jr.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 July 2003 and 28 August 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 21-25, 31-37 and 39-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 21-25, 31-37 and 39-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/28/03 has been entered.

The 35 USC § 112 first paragraph rejection is hereby dropped in view of applicants' declaration and arguments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9-12, 21-25, 31-37 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gloger, et al. (BG) in view of either of Davis, et al. (A) or Zalipsky, et al. (AY). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that "[t]he Davis patent fails to teach or suggest that coupling both linear and branched-chain polyethylene glycol to a polypeptide reduces the antigenicity of the conjugated polypeptide...[and that it] in fact teaches that branched polymers generate an immunogenic response when bound to a polypeptide", citing col. 2, line 43-48, and that therefore

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"[t]hose of ordinary skill in the art...would not have been motivated to conjugate uricase to straight or branched-chain polyethylene glycol". It is not seen the instant reference teaches that using straight chain PEG would reduce the antigenicity and it is pointed out that the instant claims are not drawn to branched polymers. Applicants state that page 8 of the specification states that the PEG may be branched or straight but this is not in the claims. Therefore the instant argument does not apply to the claims in question.

Applicants further state that on page 360 of Zapilisky, et al. it is stated that "when adenosine deaminase was conjugated to polyethylene glycol, 'no reduction of the immunogenicity was reported'". The examiner does not find this recitation on page 360. They also state that "the reference also reports that conjugation of *E. coli* asparaginase to PEG 5000 showed a reduction in antigenicity [sic], while conjugation of the enzyme to PEG 750 and PEG 1800 'did not show a substantial change of the immunogenic properties' (see page 361)". It is pointed out that the instant claims are limited to PEG of 12,000-30,000 so this argument is not pertinent to the claims. This particular teaching would appear to teach that very low MW PEG does not always reduce antigenicity. They finally argue that "the reference states that PEG-conjugated gulonolactone oxidase 'retained immunogenicity and reacted with preformed antibodies' (see page 362)". It is not clear what MW the two PEGs that were used with this enzyme were. It is further argued that the reference "fails to teach or suggest that coupling polyethylene glycol to a polypeptide necessarily increases the circulating half-life of the conjugate", again quoting the teaching regarding gulonolactone oxidase. They then argue that because of these teachings "[t]hose of ordinary skill in the art, therefore, would not have been motivated to combine the teachings of the Glo-

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ger patent with those of the Zalipsky reference...[and would not] have had a reasonable expectation of success for this combination". Applicants are pointing out exceptions that presumably do not fall within the limitations of the instant claims as to MW of PEG, but the general teaching of Zalipsky, et al. can be found in the second paragraph of page 347 where it is stated that "[i]t has been repeatedly demonstrated that covalent attachment of multiple strands of PEG to proteins produces conjugates with dramatically reduced immunogenicity and antigenicity. Such preparations also show great resistance to proteolytic digestion, and remain present in the bloodstream a considerably longer time than the parent polypeptides". This teaching alone would have been motivation for one of ordinary skill in the art to conjugate PEG with uricase with at least a reasonable expectation of success. That is all that is required under 35 USC § 103 (*In re Longi*, 225 USPQ 645 (Fed. Cir. 1985)).

Claims 1-5, 8-12, 21-25, 31-37 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chua, et al. (AB) in view of either of Davis, et al. (A) or Zalipsky, et al. (AY). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants incorporate there arguments regarding Davis, et al. and Zalipsky, et al. and state that there would be a reasonable expectation of success in combining the references. Applicants' arguments concerning these two references are addresses *supra* and therefore the rejection is repeated.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose

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telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
October 27, 2003